Note

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Susumu Nonomura and Yoshio Hirose : Synthesis of 2-Methyl-3,5,7-trimethoxyanthraquinone.

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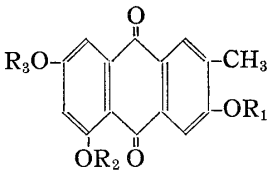
As a part of synthetic studies on the derivatives of naturally occurring anthraquinones having three hydroxyl groups, such as juzunal,[1] 2-methyl-3,5,7-trimethoxyanthraquinone (I) was synthesized.



(I) $R_1=R_2=R_3=CH_3$
(II) $R_1=CH_3$, $R_2=R_3=H$
(III) $R_1=R_2=H$, $R_3=CH_3$

2-Methyl-3-methoxy-5,7-dihydroxyanthraquinone (II), m.p. 270~272°, was obtained as a condensation product of 3,5-dihydroxybenzoic acid (IV) and 3-methoxy-4-methylbenzoic acid (V). It is evident that carboxyl group of (IV) has condensed at the 6-position in (V). On treatment with diazomethane and further, without purification, with dimethyl sulfate and potassium carbonate in acetone, (II) formed (I)[*2], m.p. 263~264°.

Experimental

2-Methyl-3-methoxy-5,7-dihydroxyanthraquinone (II)——A mixture of 3,5-dihydroxybenzoic acid (IV) (1 g.), 3-methoxy-4-methylbenzoic acid (V) (1 g.), B_2O_3 (1 g.), and conc. H_2SO_4 (2 cc.) was heated in an oil bath at 135~140° for 15 min. with intermittent shaking. After some cooling, the reaction mixture was poured into water, the precipitate was washed with water, dried, and extracted several times with benzene. After evaporation of the solvent, the residue was chromatographed on filter paper (Toyo Roshi No. 50) using BuOH saturated with 28% NH_4OH as the developing solvent. From the spot at Rf 0.57, fine orange-yellow needles (II), m.p. 270~272° (from hydr. Me_2CO), were obtained. Yield, 0.1 g. *Anal.* Calcd. for $C_{16}H_{12}O_5$: C, 67.60; H, 4.26. Found : C, 67.58; H, 4.18. IR ν_{max}^{Nujol} cm^{-1}: 1678 (non-chelated >C=O), 1642 (chelated >C=O), 1618, 1600 (phenyl).

2-Methyl-3,5,7-trimethoxyanthraquinone (I)——Me_2CO-Et_2O (300:40 cc.) solution of (II) (0.1 g.) and CH_2N_2, prepared from $CH_3N(NO)CONH_2$ (4 g.), was allowed to stand overnight at a room temperature. After evaporation of the solvent, the residue dissolved in Me_2CO (60 cc.) was refluxed with Me_2SO_4 (1 cc.) and anhyd. K_2CO_3 (2 g.) for 8 hr. After filtration, the solvent was evaporated, the residue was warmed on a water bath with 5% KOH solution, and crystallized from Me_2CO to pale yellow needles, m.p. 263~264°, (50 mg.). *Anal.* Calcd. for $C_{18}H_{16}O_5$: C, 69.22; H, 5.16. Found: C, 68.77; H, 5.43. IR ν_{max}^{Nujol} cm^{-1} : 1669 (non-chelated >C=O), 1605, 1575 (phenyl).

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*2 (III) had been assigned to the structure of macrosporin, an orange-yellow pigment found in the metabolic products of *Macrosporium porri* Elliott by R. Suemitsu, *et al.* (Bull. Agr. Chem. Soc. Japan, **21**, 1, 333 (1957); **23**, 547 (1959)). By the good offices of Mr. R. Suemitsu, infrared spectra and melting points of (I) were directly compared and found to be identical with his sample derived from natural macrosporin (III).

1) Y. Hirose : This Bulletin, **8**, 417 (1960).